Fig. 1

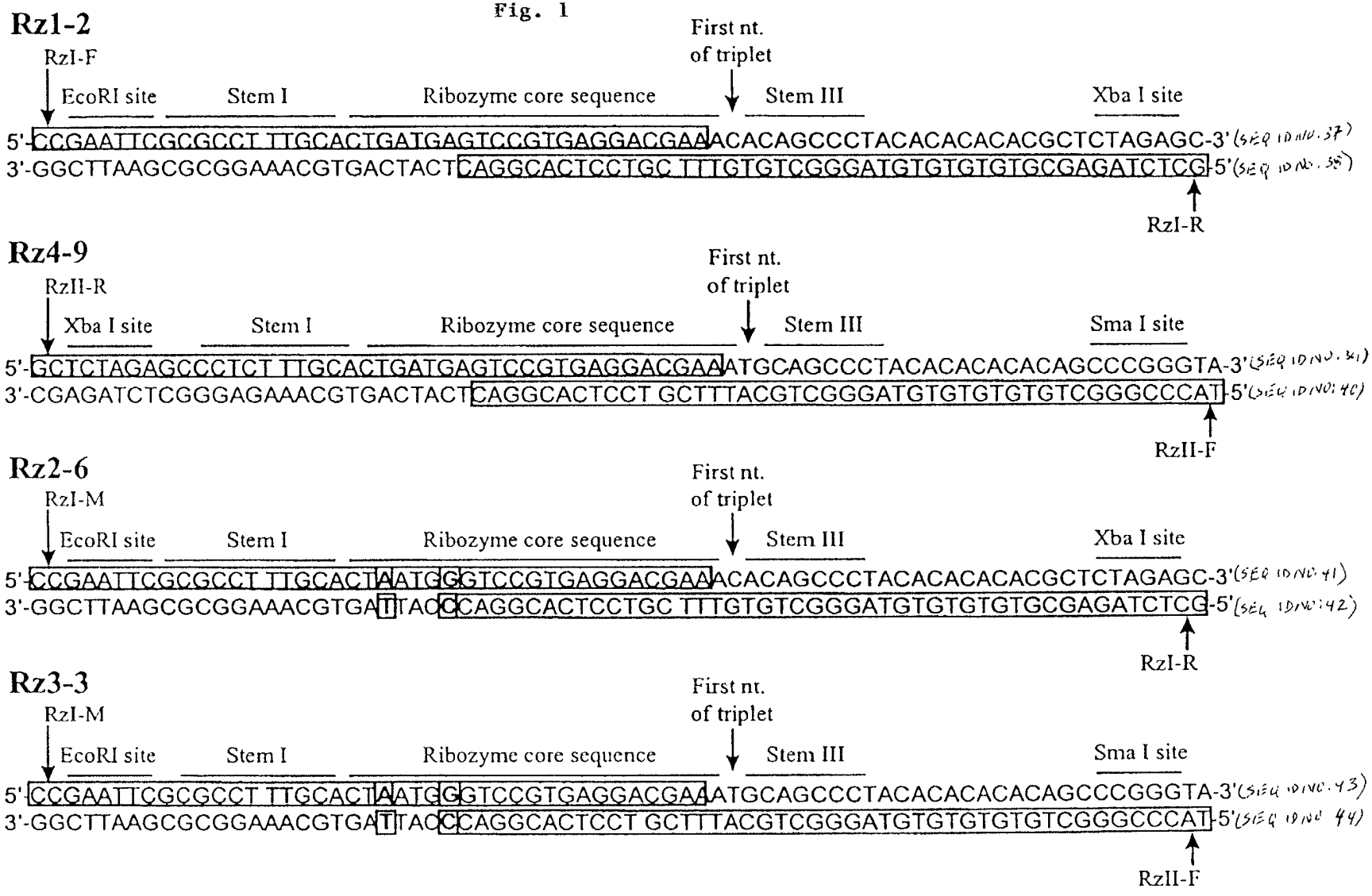

Rz1-2
RzI-F
First nt.
of triplet
EcoRI site
Stem I
Ribozyme core sequence
Stem III
Xba I site
5'-CCGAATTCGCGCCT TTGCACTGATGAGTCCGTGAGGACGAAACACAGCCCTACACACACACGCTCTAGAGC-3' (SEQ ID NO. 37)
3'-GGCTTAAGCGCGGAAACGTGACTACTCAGGCACTCCTGC TTTGTGTCGGGATGTGTGTGTGCGAGATCTCG-5' (SEQ ID NO. 38)
RzI-R
Rz4-9
RzII-R
First nt.
of triplet
Xba I site
Stem I
Ribozyme core sequence
Stem III
Sma I site
5'-GCTCTAGAGCCCTCT TTGCACTGATGAGTCCGTGAGGACGAAATGCAGCCCTACACACACACAGCCCGGGTA-3' (SEQ ID NO. 39)
3'-CGAGATCTCGGGAGAAACGTGACTACTCAGGCACTCCT GCTTTACGTCGGGATGTGTGTGTGTCGGGCCCAT-5' (SEQ ID NO: 40)
RzII-F
Rz2-6
RzI-M
First nt.
of triplet
EcoRI site
Stem I
Ribozyme core sequence
Stem III
Xba I site
5'-CCGAATTCGCGCCT TTGCACTAATGGGTCCGTGAGGACGAAACACAGCCCTACACACACACGCTCTAGAGC-3' (SEQ ID NO: 41)
3'-GGCTTAAGCGCGGAAACGTGATTACCCAGGCACTCCTGC TTTGTGTCGGGATGTGTGTGTGCGAGATCTCG-5' (SEQ ID NO: 42)
RzI-R
Rz3-3
RzI-M
First nt.
of triplet
EcoRI site
Stem I
Ribozyme core sequence
Stem III
Sma I site
5'-CCGAATTCGCGCCT TTGCACTAATGGGTCCGTGAGGACGAAATGCAGCCCTACACACACACAGCCCGGGTA-3' (SEQ ID NO. 43)
3'-GGCTTAAGCGCGGAAACGTGATTACCCAGGCACTCCT GCTTTACGTCGGGATGTGTGTGTGTCGGGCCCAT-5' (SEQ ID NO 44)
RzII-F

Fig. 2A

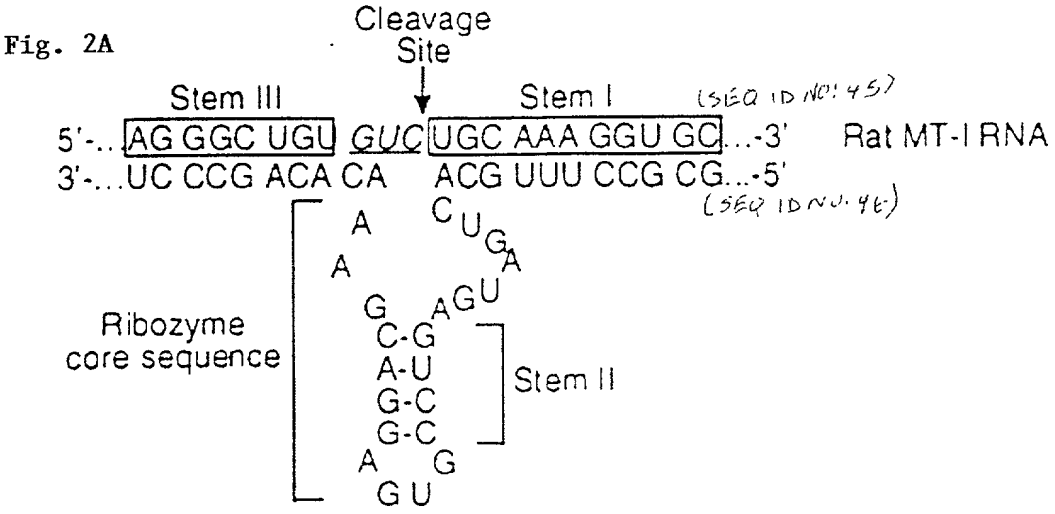

Cleavage Site
Stem III
Stem I
(SEQ ID NO: 45)
5'-.. AG GGC UGU GUC UGC AAA GGU GC...-3'
Rat MT-I RNA
3'-...UC CCG ACA CA ACG UUU CCG CG...-5'
(SEQ ID NO. 46)
Ribozyme core sequence
Stem II
C-G
A-U
G-C
G-C

Fig. 2B

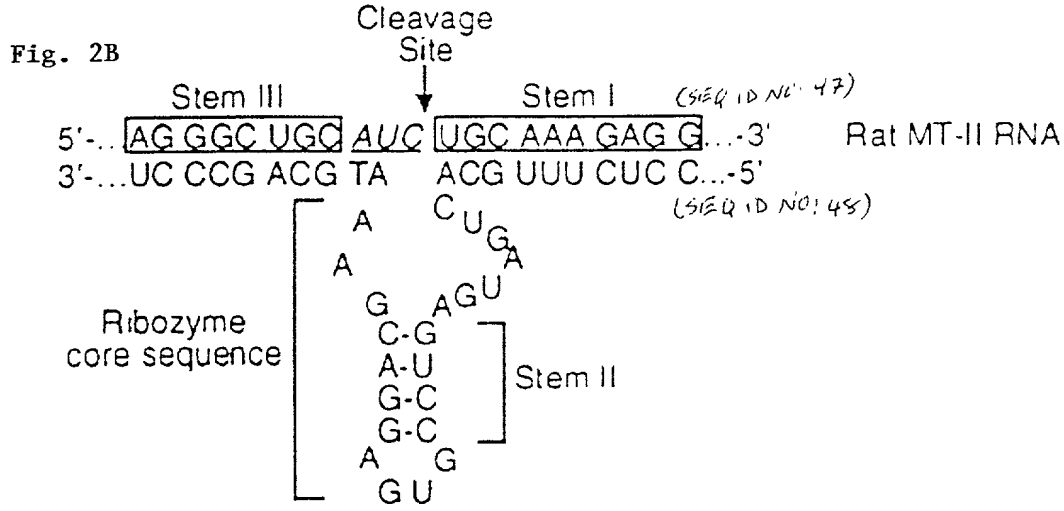

Cleavage Site
Stem III
Stem I
(SEQ ID NO: 47)
5'-.. AG GGC UGC AUC UGC AAA GAG G...-3'
Rat MT-II RNA
3'-...UC CCG ACG TA ACG UUU CUC C...-5'
(SEQ ID NO: 48)
Ribozyme core sequence
Stem II
C-G
A-U
G-C
G-C

Fig. 3

Sequence Comparison between Rodent and Human MT Messages on the Regions Recognized by Ribozymes (MT-I Rz, upper; MT-II Rz, lower) and Their Cleavage Triplets

Gene	Accession No. (NCBI GenBank)	AGGGCTGT Stem III −nt 137–144 (8 nt)	GTC Cleavage triplet −nt. 145–147	TGCAAAGGCGC Stem I −nt. 148–158 (11 nt)	Expected effectiveness
MT-I Rz (Rz1-2)					
Mouse MT-I	S62785	PM	PM	PM	+
Rat MT-I	M11794	PM	PM	C → T (nt. 156)	+
Human MT-Ib	M13485	PM	PM	G → T (nt. 157)	+
Human MT-Ie	M10942	T → C (nt. 144)*	PM	C → G (nt. 156)	−
Human MT-If	M10943	PM	C → T (nt. 147)*	C → G (nt. 156)	−
Human MT-Ir	X97261	T → C (nt. 144)*	PM	C → G (nt. 156)	−
MT-II Rz (Rz4-9)					
Mouse MT-II	K02236	PM	PM	PM	+
Rat MT-II	M11794	PM	PM	PM	+
Human MT-II	M26637	PM	PM	A → G (nt. 155)	+
Human MT-Ia	K01383	PM	C → G (nt. 147)*	A → G (nt. 155)	−
Human MT-Ie	M10942	PM	A → G (nt. 145)*	A → G (nt. 155)	−
Human MT-Ig	J03910	G → A (nt. 138)	PM	A → G (nt. 155)	+
Human MT-Ih	X64834	PM	PM	A → G (nt. 155)	+
Human MT-Il	X76717	PM	PM	A → G (nt. 155)	+
Human MT-Ir	X97261	PM	A → G (nt. 145)*	A → G (nt. 155)	−
Human MT-Ix	X65607	PM	PM	A → G (nt. 155)	+

Fig. 4

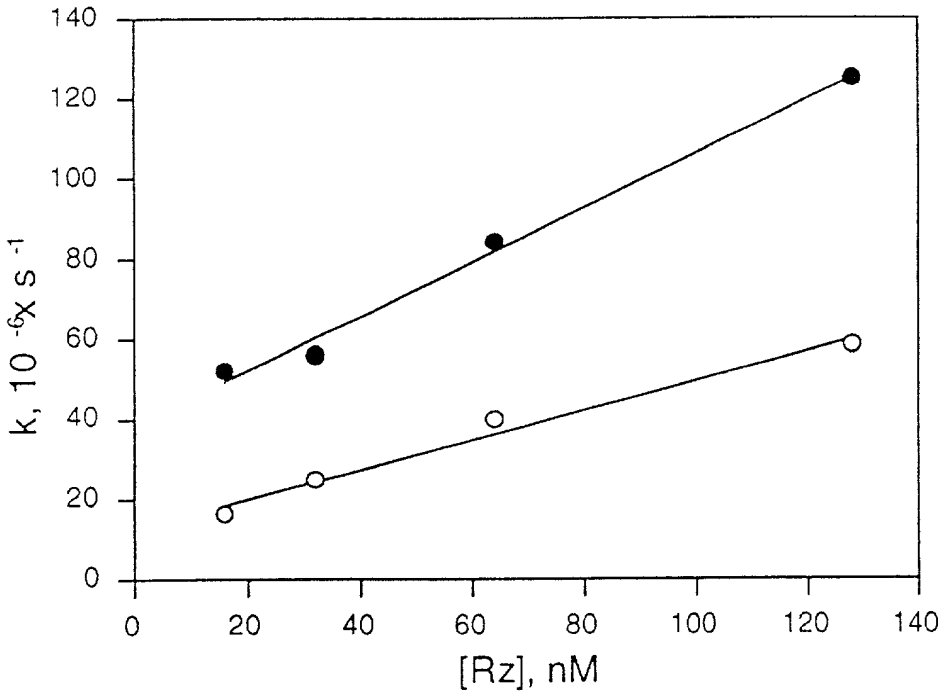


Fig. 5

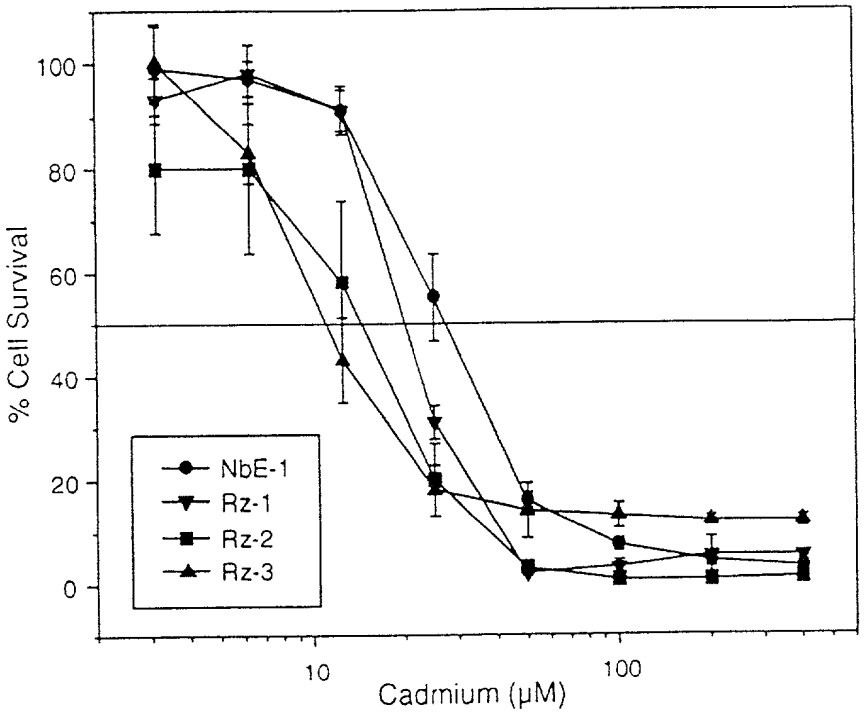

100
80
60
40
20
0
% Cell Survival
NbE-1
Rz-1
Rz-2
Rz-3
10
100
Cadmium (μM)

Fig. 6

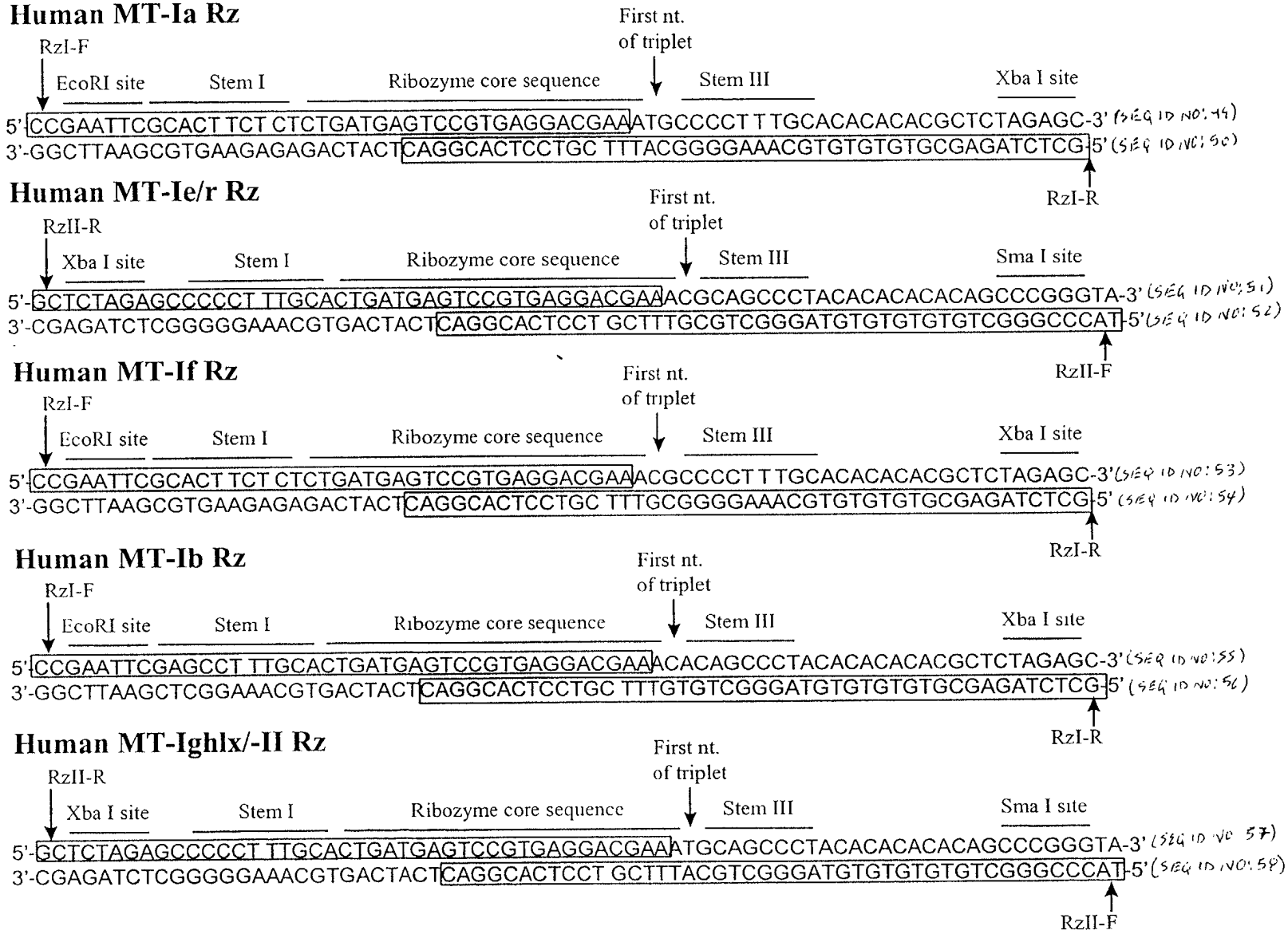

Human MT-Ia Rz
RzI-F
First nt. of triplet
EcoRI site
Stem I
Ribozyme core sequence
Stem III
Xba I site
5'-CCGAATTCGCACT TCT CTCTGATGAGTCCGTGAGGACGAAATGCCCCT T TGCACACACACGCTCTAGAGC-3' (SEQ ID NO: 49)
3'-GGCTTAAGCGTGAAGAGAGACTACTCAGGCACTCCTGC TTTACGGGGAAACGTGTGTGTGCGAGATCTCG-5' (SEQ ID NO: 50)
RzI-R
Human MT-Ie/r Rz
RzII-R
First nt. of triplet
Xba I site
Stem I
Ribozyme core sequence
Stem III
Sma I site
5'-GCTCTAGAGCCCCCT TTGCACTGATGAGTCCGTGAGGACGAAACGCAGCCCTACACACACACAGCCCGGGTA-3' (SEQ ID NO: 51)
3'-CGAGATCTCGGGGGAAACGTGACTACTCAGGCACTCCT GCTTTGCGTCGGGATGTGTGTGTGTCGGGCCCAT-5' (SEQ ID NO: 52)
RzII-F
Human MT-If Rz
RzI-F
First nt. of triplet
EcoRI site
Stem I
Ribozyme core sequence
Stem III
Xba I site
5'-CCGAATTCGCACT TCT CTCTGATGAGTCCGTGAGGACGAAACGCCCCT T TGCACACACACGCTCTAGAGC-3' (SEQ ID NO: 53)
3'-GGCTTAAGCGTGAAGAGAGACTACTCAGGCACTCCTGC TTTGCGGGGAAACGTGTGTGTGCGAGATCTCG-5' (SEQ ID NO: 54)
RzI-R
Human MT-Ib Rz
RzI-F
First nt. of triplet
EcoRI site
Stem I
Ribozyme core sequence
Stem III
Xba I site
5'-CCGAATTCGAGCCT TTGCACTGATGAGTCCGTGAGGACGAAACACAGCCCTACACACACACGCTCTAGAGC-3' (SEQ ID NO: 55)
3'-GGCTTAAGCTCGGAAACGTGACTACTCAGGCACTCCTGC TTTGTGTCGGGATGTGTGTGTGCGAGATCTCG-5' (SEQ ID NO: 56)
RzI-R
Human MT-Ighlx/-II Rz
RzII-R
First nt. of triplet
Xba I site
Stem I
Ribozyme core sequence
Stem III
Sma I site
5'-GCTCTAGAGCCCCCT TTGCACTGATGAGTCCGTGAGGACGAAATGCAGCCCTACACACACACAGCCCGGGTA-3' (SEQ ID NO: 57)
3'-CGAGATCTCGGGGGAAACGTGACTACTCAGGCACTCCT GCTTTACGTCGGGATGTGTGTGTGTCGGGCCCAT-5' (SEQ ID NO: 58)
RzII-F

Fig. 7A

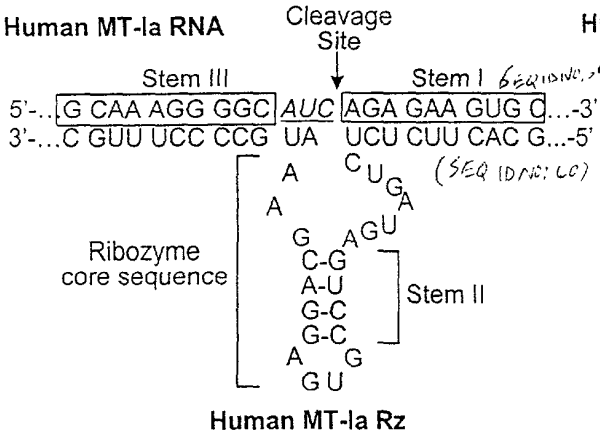


Fig. 7B

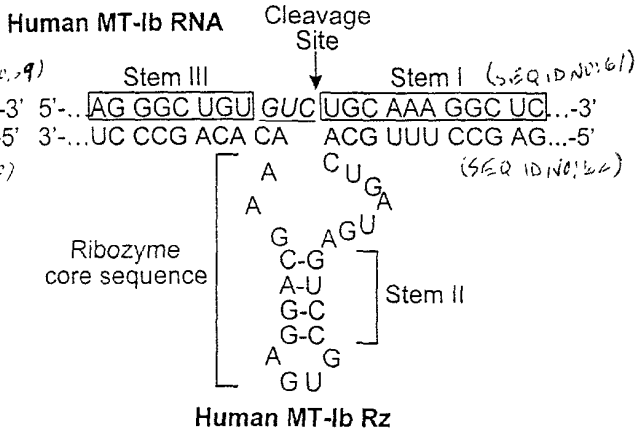


Fig. 7C

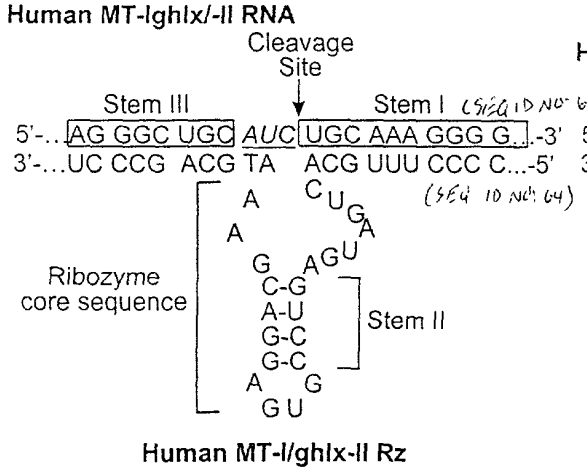


Fig. 7D

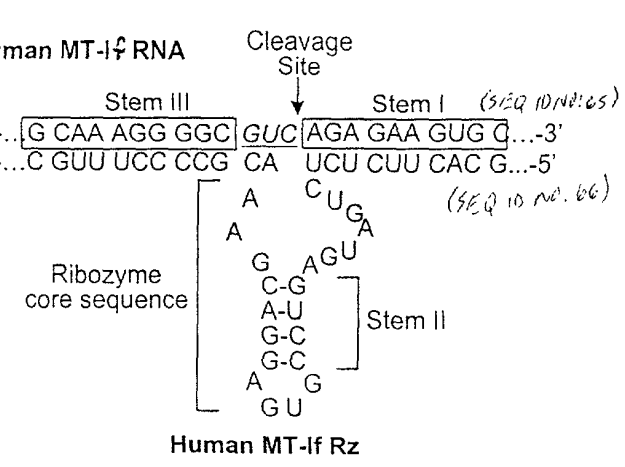


Fig. 7E

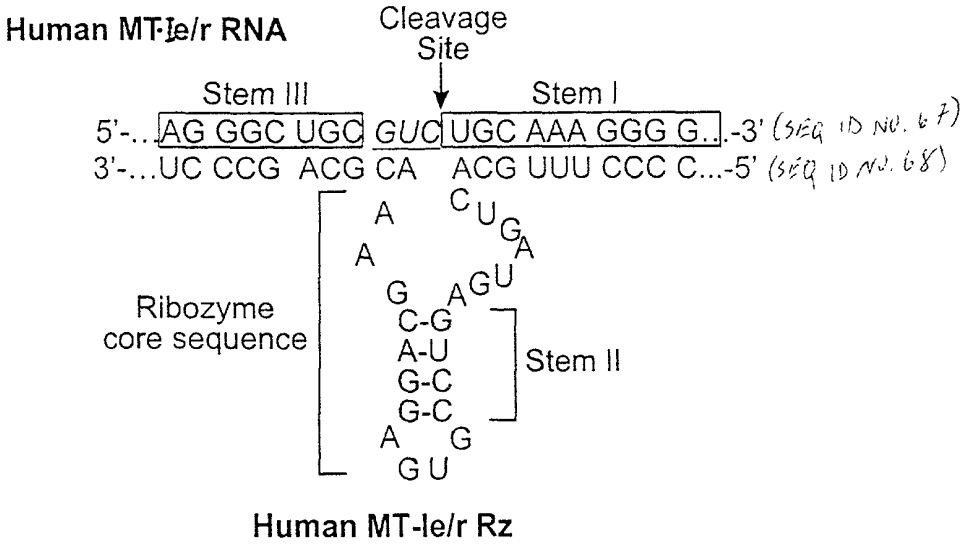
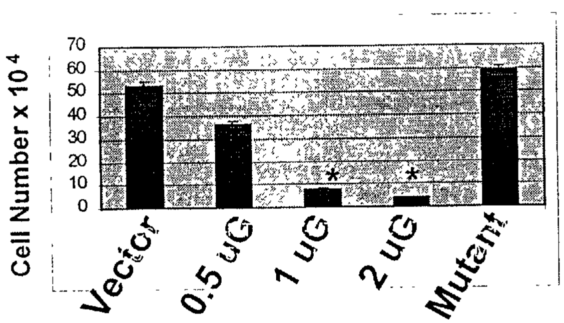

Human MT-Ie/r RNA
Cleavage Site
Stem III
Stem I
5'-..AG GGC UGC GUC UGC AAA GGG G..-3' (SEQ ID NO. 67)
3'-...UC CCG ACG CA ACG UUU CCC C...-5' (SEQ ID NO. 68)
Ribozyme core sequence
C-G
A-U
G-C
G-C
Stem II
Human MT-Ie/r Rz

Fig. 8A



* = P < 0.005

Fig. 8B

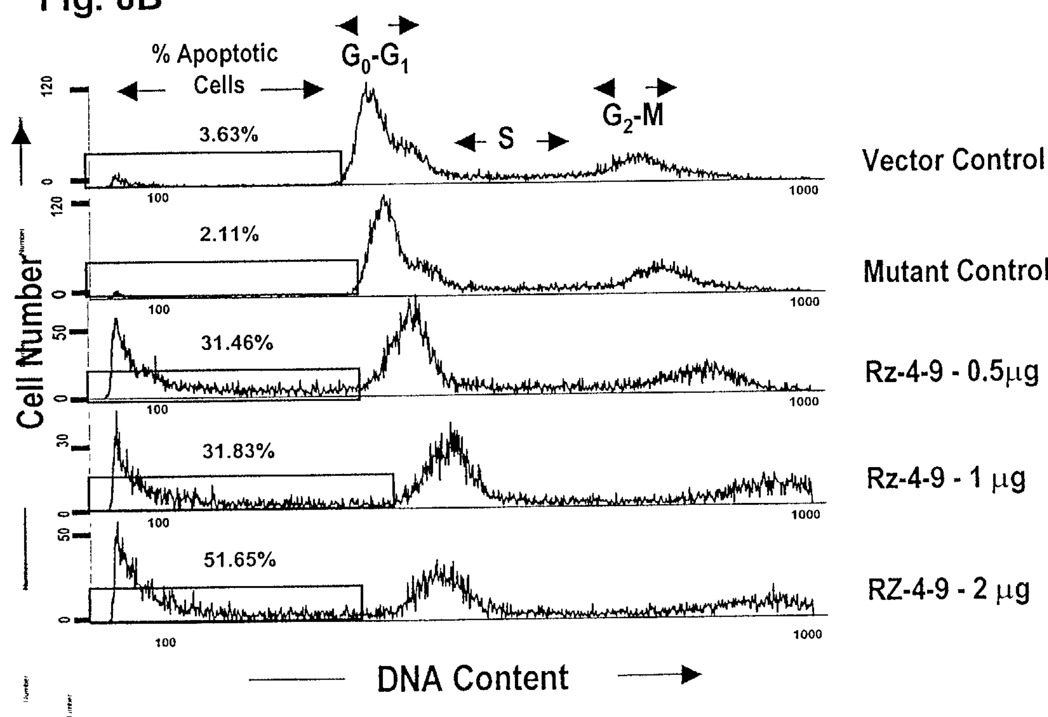
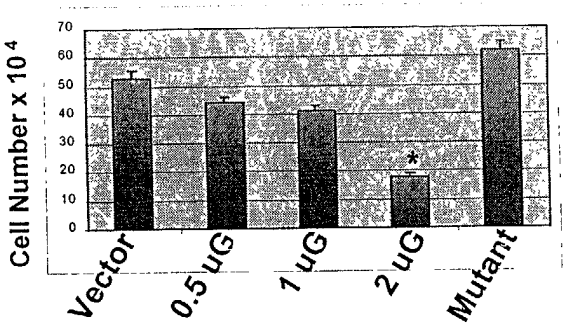


Fig. 9A



* = P < 0.005

Fig. 9B

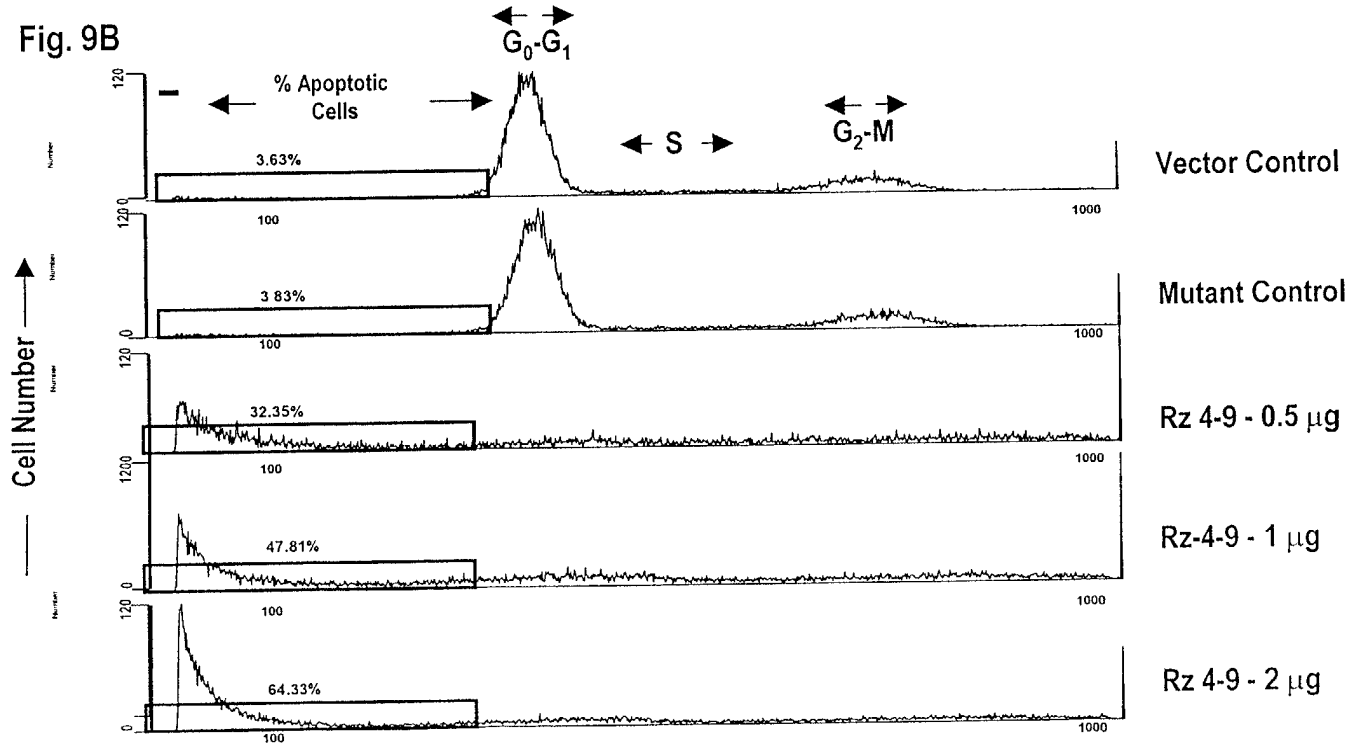


Fig. 10A

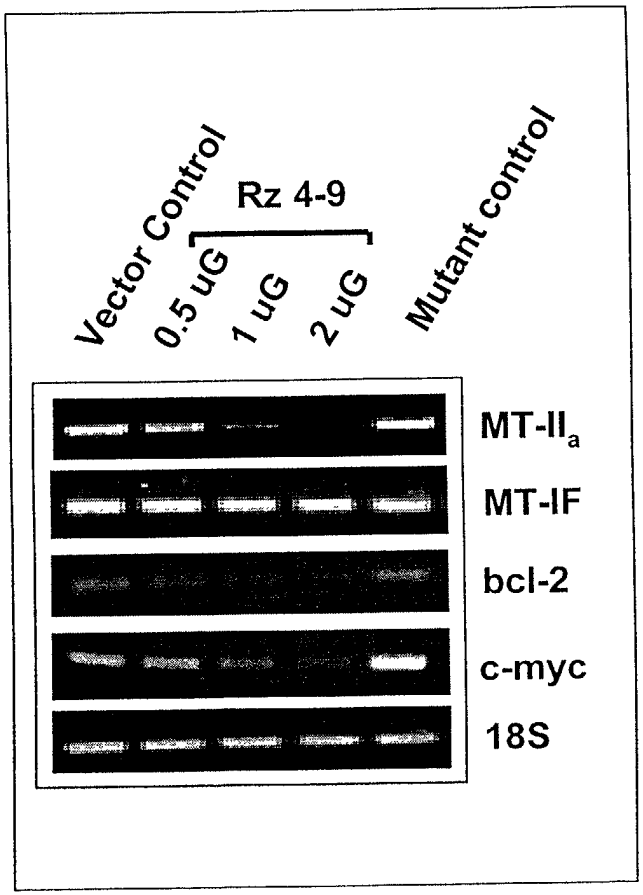
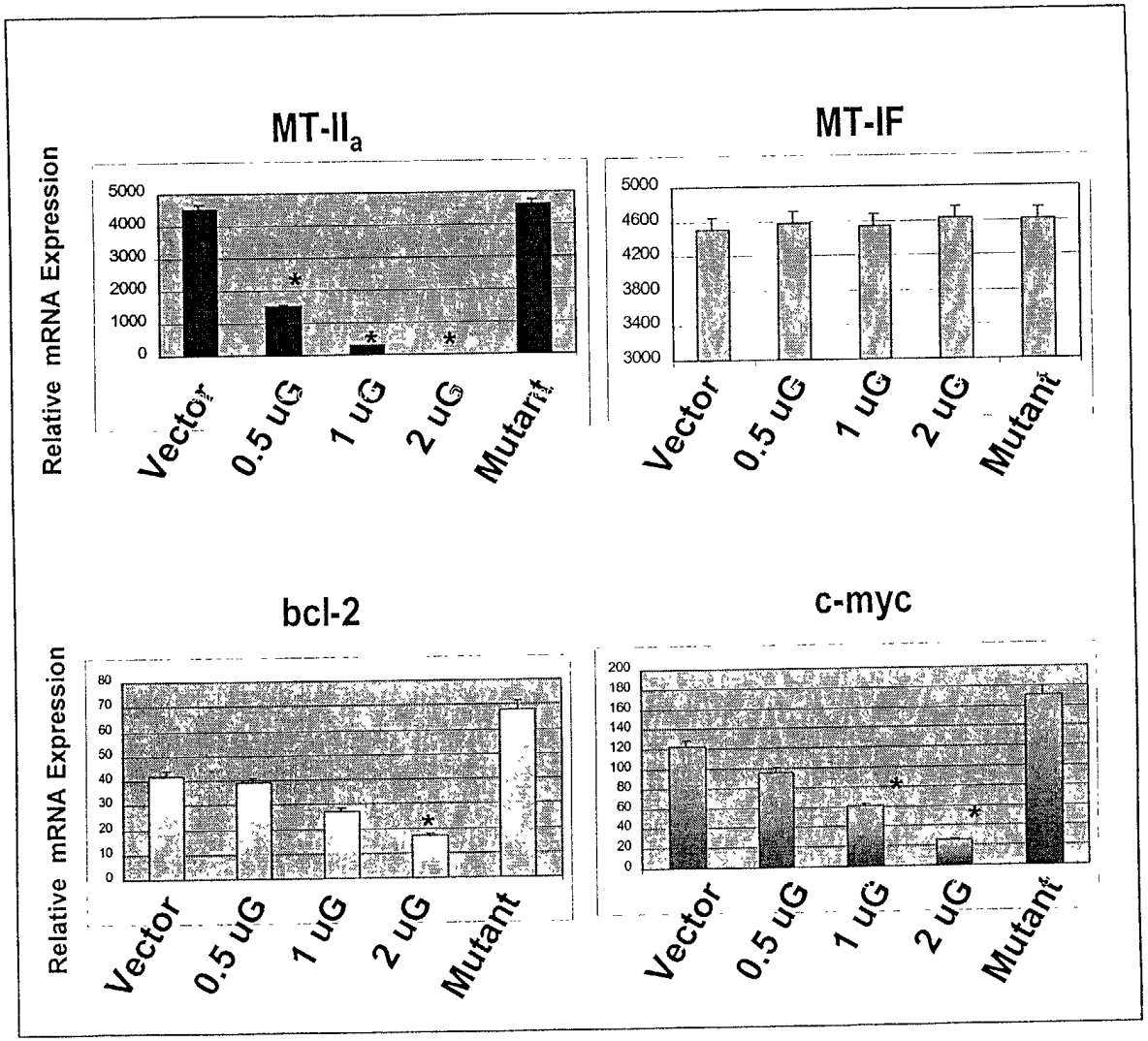


Fig. 10B



* = P < 0.005

Fig. 11A

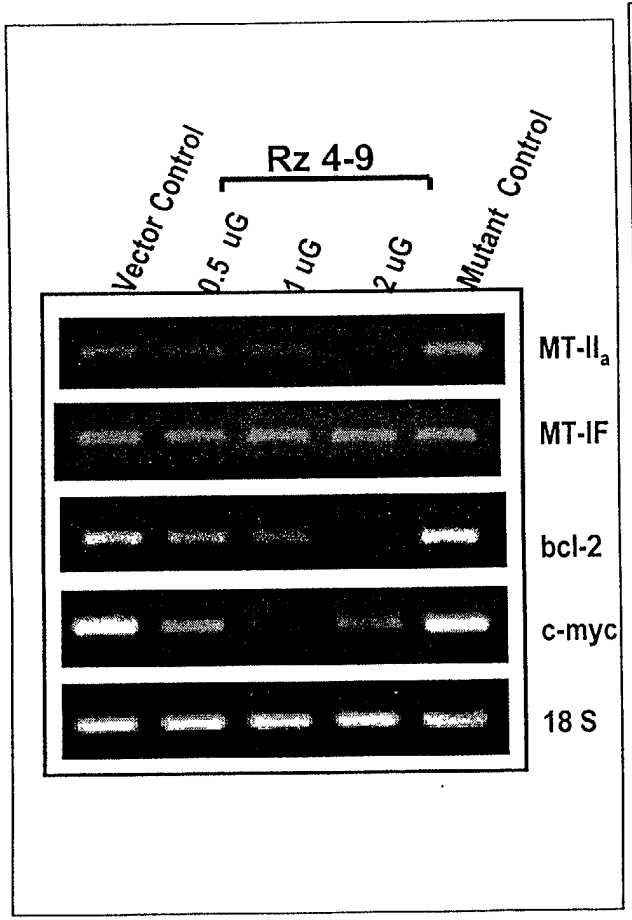
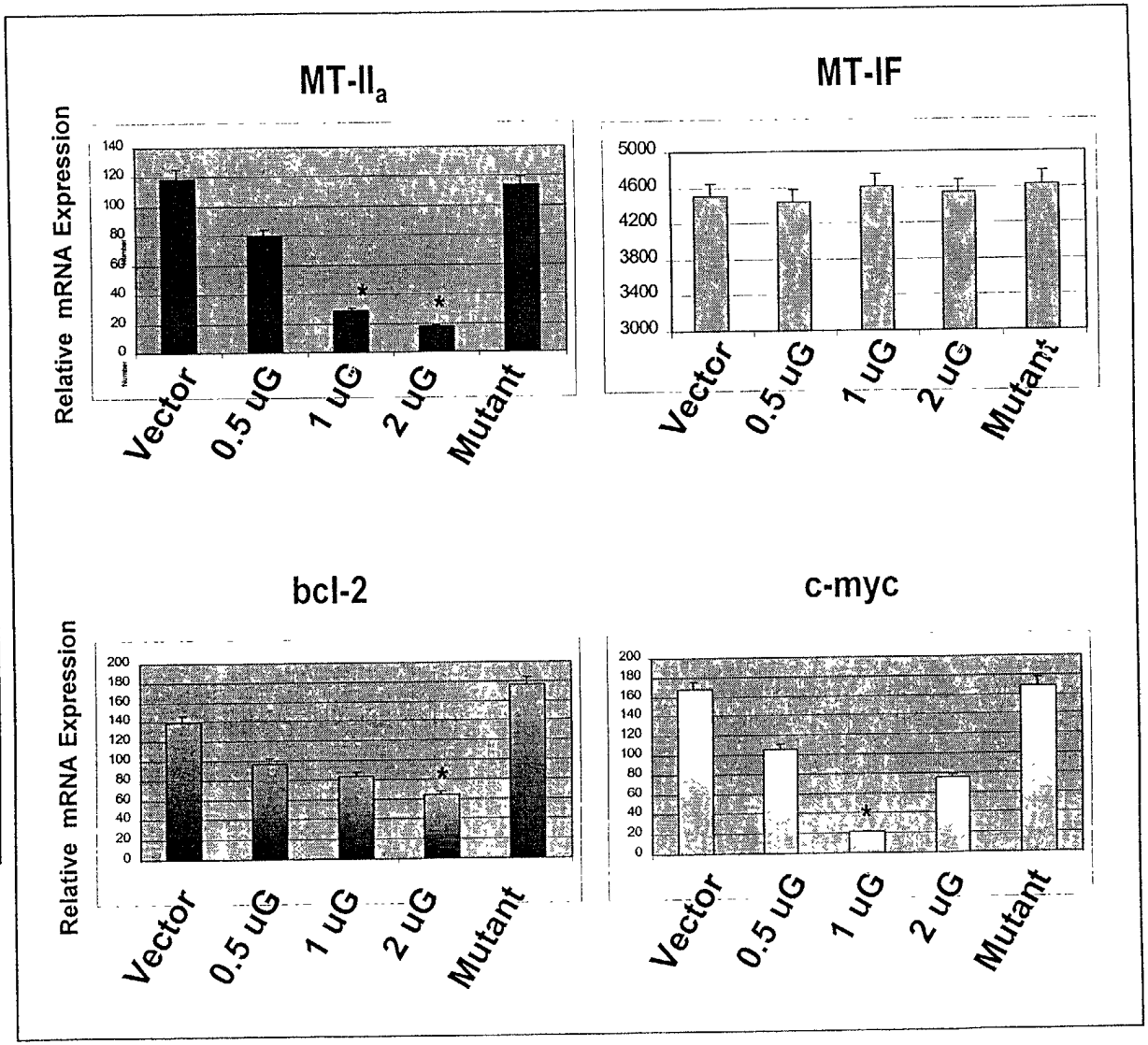


Fig. 11B



* = P < 0.005

Fig. 12A

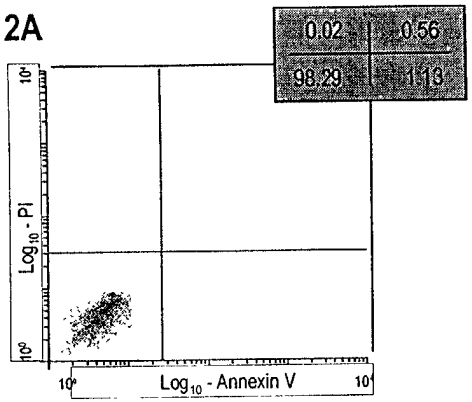


Fig. 12B

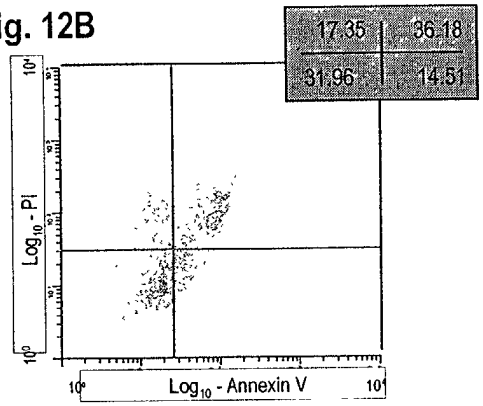


Fig. 12C

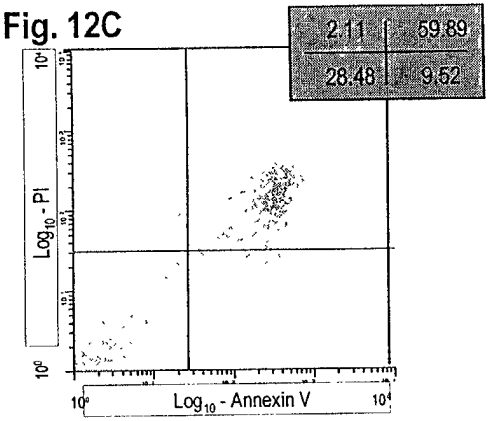


Fig. 12D

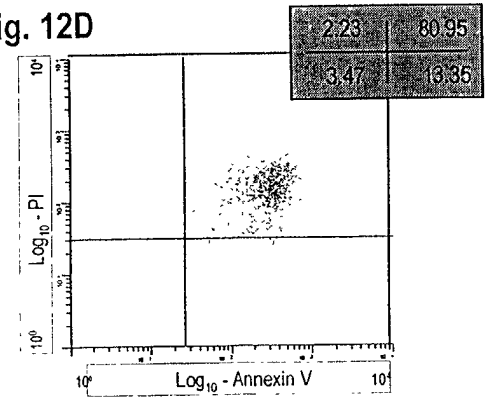


Fig. 12E

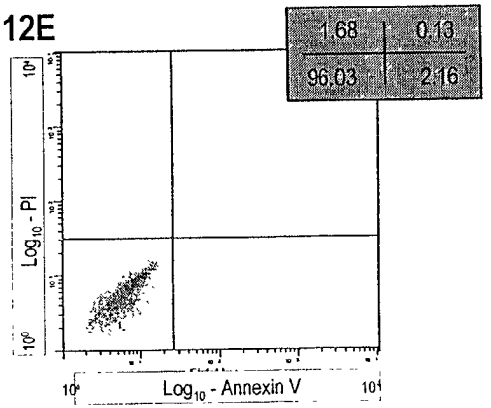


Fig. 13A

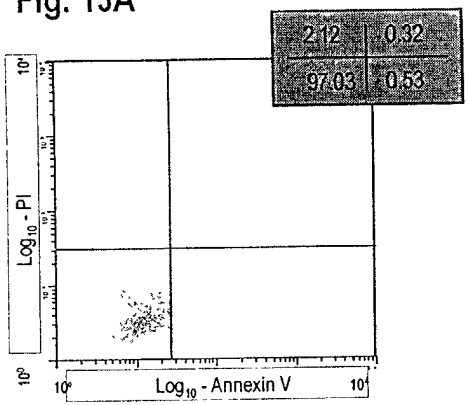


Fig. 13B

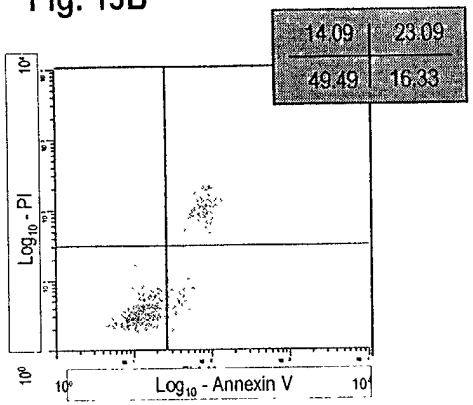


Fig. 13C

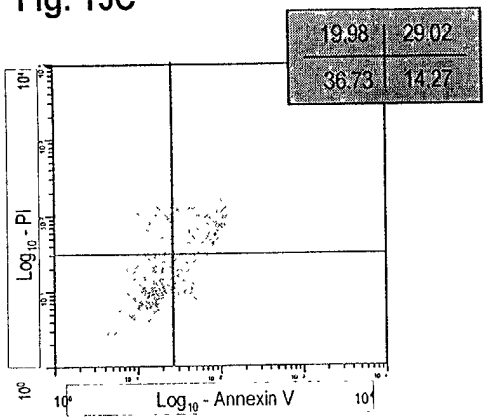


Fig. 13D

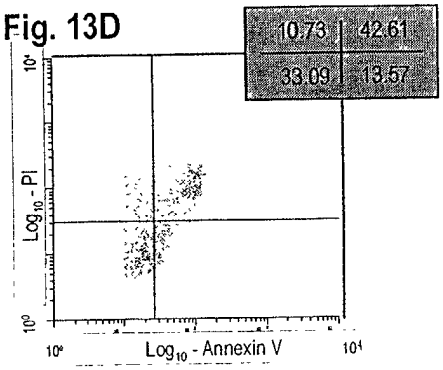


Fig. 13E

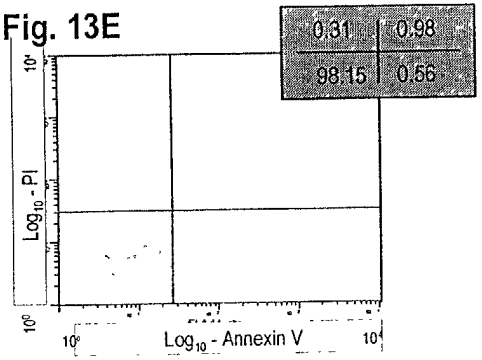


Fig. 14

Human MT-Ia Rz:
Forward Primer: 5'-CCG AAT TCG CAC TTC TCT CTG ATG AGT CCG TGA GGA CGA A-3' (SEQ ID NO: 27)
Reverse Primer: 5'-GCT CTA GAG CGT GTG TGT GCA AAG GGG CAT TTC GTC CTC ACG GAC-3' (SEQ ID NO: 28)

Human MT-If Rz:
Forward Primer: 5'-CCG AAT TCG CAC TTC TCT CTG ATG AGT CCG TGA GGA CGA A-3' (SEQ ID NO: 29)
Reverse Primer: 5'-GCT CTA GAG CGT GTG TGT GCA AAG GGG CGT TTC GTC CTC ACG GAC-3' (SEQ ID NO: 30)

Human MT-Ie/r Rz:
Forward Primer: 5'-TAC CCG GGC TGT GTG TGT GTA GGG CTG CGT TTC GTC TCA CGG AC-3' (SEQ ID NO: 31)
Reverse Primer: 5'-GCT CTA GAG CCC CCT TTG CAC TGA TGA GTC CGT GAG GAC GAA-3' (SEQ ID NO: 32)

Human MT-Ighlx/-II Rz:
Forward Primer: 5'-GCT CTA GAG CCC CCT TTG CAC TGA TGA GTC CGT GAG GAC GAA-3' (SEQ ID NO: 33)
Reverse Primer: 5'-TAC CCG GGC TGT GTG TGT GTA GGG CTG CAT TTC GTC CTC ACG GAC-3' (SEQ ID NO: 34)

Human MT-Ib Rz:
Forward Primer: 5'- CCG AAT TCG AGC CTT TGC ACT GAT GAG TCC GTG AGG ACG AA-3' (SEQ ID NO: 35)
Reverse Primer: 5'-GCT CTA GAG CGT GTG TGT GTA GGG CTG TGT TTC GTC CTC ACG GAC-3' (SEQ ID NO: 36)